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Popular Article

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Bovine ketosis (acetonaemia)

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Definition

Ketosis is a metabolic disease of high-yielding animals characterized by hypoglycemia, ketonaemia and ketonuria (OR) accumulation of the abnormal number of ketone-bodies in the tissues and tissue fluids. Ketosis in ruminants is a multifactorial disorder of energy metabolism. The disease in cattle responds to treatment and is self-limiting.

Classification:

A) On the basis of cause:
1. Primary ketosis (uncomplicated ketosis): It is caused due to starvation, underfeeding, or feeding of an unbalanced diet.
2. Secondary ketosis: It is caused by various systemic or infectious diseases viz. mastitis, and pneumonia. In this type, the animal takes inadequate feed due to loss of appetite even though sufficient feed is offered.

B) On the basis of feeding status:
1) Bad season/starvation ketosis: It occurs in the dry season/summer season due to a lack of carbohydrates in the diet.
2) Good season / well fed ketosis: It occurs in well-fed animals due to the excess production of ketone bodies more than the utilization.

Epidemiology:

a) Species: Cows and buffaloes are affected.
b) Breeds: Buffaloes and crossbred cows are more susceptible than indigenous cows.
c) Sex: Primary ketosis is actually a disease of females.
d) Age: It is common in 6-9 years old animals.
e) No. of lactations: Disease incidence is higher during the 3rd to 5th lactation.
f) Physiological status: It is a disease of lactating cows and buffaloes.
g) Stage of lactation: It commonly occurs between 10 days to 2 months of calving.
h) Milk yield: High-yielding animals are more susceptible than low yielding animals.
i) Season: Incidence is higher during calving season i.e., September to December.
j) Feeding systems: It is more common in housed or stall-fed animals.
k) Morbidity: Variable
l) Mortality: Very low
m) Predisposing factors: Genetic susceptibility, Cold stress.
n) Economic importance: Loss of milk production up to 25-100%**.** About 30 - 40% of cases are complicated by concurrent diseases like metritis, TRP, abomasal diseases, surra and theileriosis.

Etiology:

A) Dietary factors:
1) Under nutrition / Starvation or feeding of low CHO diet: This leads to decreased production of propionate, hypoglycemia, increased fat metabolism and ketone body formation.
2) Feeding of excess amount of protein-rich diet: This is responsible for increased production of ketogenic acids like butyric acid.
3) Excess feeding of silage: Silage produces more butyrate and sometimes silage itself contains 2 – 4% butyrate.
4) Deficiency of cobalt and phosphorus: Cobalt deficiency results into failure to metabolize propionic acid whereas phosphorus deficiency may lead to decreased feed intake.

B) Animal factors:
1) High milk yield: Heavy drain of lactose through milk leads to negative energy balance.
2) Lack of exercise: This leads to decreased oxidation i.e. utilization of ketone bodies by muscles.
3) Hepatic insufficiency: The glycogen is stored in the liver and it is converted to glucose in emergencies by hepatic cells. But in hepatic insufficiency, there is insufficient conversion of glycogen to glucose leading to hypoglycemia.
C) Hormonal factors:
1) Hypothyroidism: It may be a contributory factor. The thyroid hormone promotes gluconeogenesis. Hence gluconeogenesis is hampered in hypothyroidism.
2) Adreno-cortical insufficiency: In stress, the adrenal cortex secretes glucocorticoids which stimulate gluconeogenesis. The adrenal cortex may get exhausted due to overactivity in stress such as pregnancy and parturition. In the absence of gluco-corticoides gluconeogenesis does not occur.
3) Insulin deficiency: It leads to decreased utilization of glucose and increased lipolysis.
D) Environmental factor: Exposure to cold climate –may be a contributory factor.
E) Systemic and infectious diseases responsible for loss of appetite: Metritis, mastitis, pneumonia, surra, thieleriosis, TRP and abomasal displacement.

Normal ketone body metabolism:

The ruminants absorb very little dietary carbohydrates such as hexose sugar because dietary CHO is fermented in the rumen to short-chain fatty acids, principally, acetate, propionate and butyrate. They have produced in an approximate 70: 20: 10 ratio. Acetate is condensed to body/milk fat provided glucose metabolism is going on. Acetate is utilized for energy production via the TCA cycle provided oxaloacetate is present. Acetate is converted to ketone bodies viz. Acetoacetate, acetone and β-hydroxy butyrate if oxaloacetate is deficient. FFA produced from the mobilization of fat is transported to the liver and oxidized to produce acetyl-COA. Acetyl COA may be oxidized via the TCA cycle or metabolized to aceto-acetyl COA. Oxidation of acetyl COA via The CA cycle depends upon an adequate supply of oxaloacetate from the precursor propionate. If propionate and oxaloacetate are deficient, oxidation of acetyl COA via the TCA cycle is limited and it is metabolized to aceto-acetyl COA and subsequently to acetoacetate and β-hydroxy butyrate. Propionate is the most important glucose precursor. Propionate enters in TCA cycle at the level of succinyl COA and is utilized for the synthesis of oxaloacetate and glucose.
Acetoacetate is considered the parent ketone body.

- ✧ Acetoacetate is reduced to β-hydroxy butyric acid by the enzyme β-hydroxy butyrate dehydrogenase through an irreversible reaction.
- ✧ Acetoacetate is an unstable compound that forms acetone and CO_2 irreversibly and non-enzymatically.

Ketogenic substances:

a) All fatty acids (i.e. 90% food fat).
b) Proteins (ketogenic approximately 40%)

Anti-ketogenic substances:

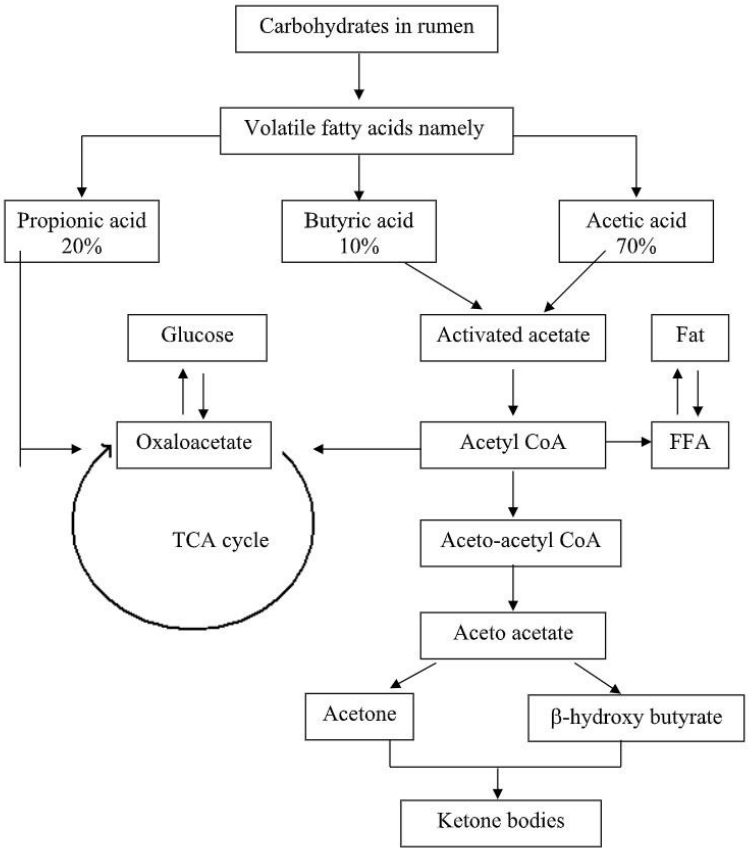
a) Carbohydrates (100%)
b) Protein (60%) – Glucogenic amino acids.
c) Fats (10%) – Glycerol

Ketone bodies arise from two major sources:

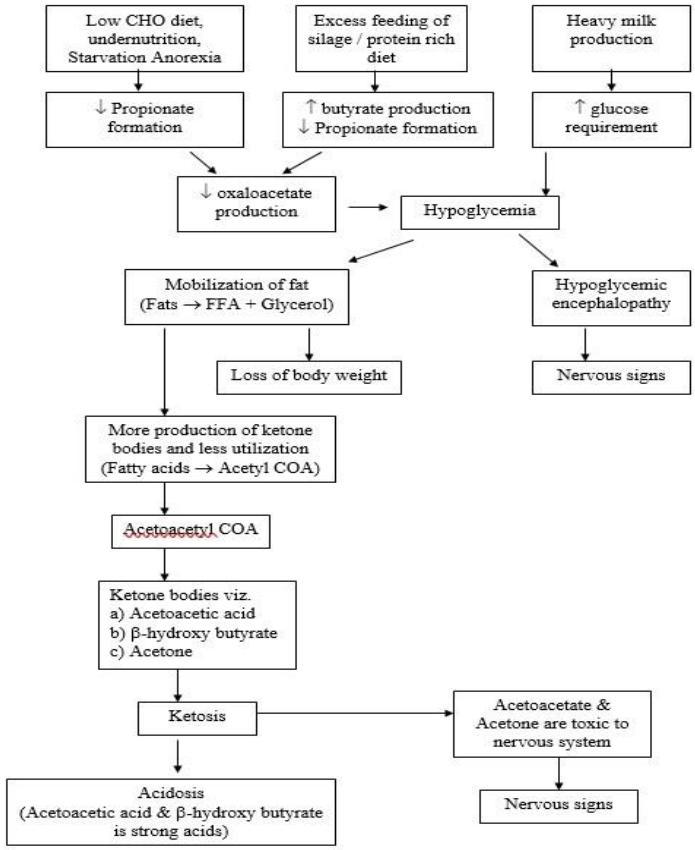
1) A large amount of butyrate produced in the rumen is converted to β-hydroxy butyrate in the ruminal epithelium and is absorbed as such.
2) Ketone bodies are produced from the mobilization of fat.

Hormonal regulation of energy metabolism:

- ✧ The energy metabolism in ruminants is primarily regulated by insulin and glucagons.
- ✧ It is also indirectly governed by somatotropin which is the most important determinant of milk yield in cattle and lipolytic.



Pathogenesis :



[The nervous signs occur in some cases of ketosis may be caused by →
- ✧ Isopropyl alcohol, a breakdown product of acetoacetic acid in the rumen.
- ✧ Hypoglycemia.

Clinical signs:

Ketosis can be grouped as clinical and sub-clinical ketosis based on the presence or absence of signs.

A) Clinical ketosis: It mainly occurs in two forms.

1) Digestive / wasting form:

It is the most common form of ketosis. Selective appetite: Refusal of concentrates. A marked drop in milk yield (25 – 100%)**.** Emaciation / woody appearance due to rapid loss of body weight. Moderate depression and disinclination to move. Loss of skin elasticity (due to the disappearance of sub-cut fat)**.** Dull skin and rough body coat. Feces are firm, dry and covered with mucus. Ruminal motility is usually reduced and weak. Sweetish smell to breath, milk and urine. Body temperature, pulse and respiration are usually normal. If not treated, a few animals may die. In the remaining animals, the milk yield falls and spontaneous recovery occurs within a month but milk yield is not regained.

2) Nervous Form:

Aimless wandering. Staggering gait/crossing of legs. Circling movements – Walking in circles. Head pressing. Apparent blindness. Vigorous liking of skin and inanimate objects. Chewing movements with profuse salivation. Depraved appetite. Nervous signs like hyperaesthesia, tremors and convulsions may occur in short episodes which last for 1-2 hrs. and may occur at an interval of about 8 – 12 hrs.

B) Sub-clinical / Spontaneous Ketosis:

It occurs in high-yielding cattle due to excessive production of aceto-acetic acid in mammary glands. It may regress or remain as such or turn into clinical form. Mild drop in milk yield. Reduced fertility.

C) Milk Fever type ketosis: It is characterized by signs of hypoglycemia and hypocalcemia.

Clinical Pathology:

I) Biochemistry:

1) Blood glucose: Decreases to 20 – 40 mg/dl (Normal: 50 – 60 mg/dl)
2) Blood ketone: Increases to 20 – 100 mg/dl (Normal < 10 mg/dl)
3) Ketone bodies in urine: Increases up to 80-130 mg/dl (Normal: Little or < 10 mg/dl may be up to 70 mg/dl)
4) Milk ketone level: Increases up to 10-40 mg/dl (Normal: Not excreted, but may be up to 3 mg/dl)
5) Serum calcium: Slightly decreased
6) Serum Mg: Slightly decreased.
7) Total lipids: Increases up to 227 – 400 mg/dl
8) Cholesterol: Increases up to 111-150 mg/dl
9) Triglycerides: Increases up to 65-85 mg/dl

II) Haematology: DLC indicates Neutropenia (10%), Lymphocytosis (60-80%) and Eosinophilia (15 – 40%)

III) Urinalysis: Urine samples are positive for ketone bodies.

IV) Milk Sample: Positive for ketone bodies.

Diagnosis:

1) History: Recent calving (2 – 8 weeks post-partum), high milk yield, underfeeding of carbohydrates, excess feeding of protein-rich concentrates, exposure to cold climate.
2) Clinical findings: Selective appetite, Drop in milk production, Emaciation, Sweetish smell to breath.
3) Clinical Pathology: Hypoglycemia (< 40 mg %), Ketonemia (> 20 mg %) and Ketonusia.
4) Response to treatment: Good response to specific treatment viz. glucose therapy.

Treatment:

The rational treatment in ketosis is to relieve the need for glucose formation in tissues. Allow ketone body utilization to continue normally. This can be achieved by glucose replacement therapy. The response to treatment is good in most cases. In some cases, transient response and death in rare cases.

A) Replacement Therapy:

1) Glucose therapy:

20% Glucose @ 0.5 gm/kg I/V for 2 to 3 days. It relieves the need for glucose and allows one to utilize the ketone body.

2) Fructose / Xylitol or a mixture of glucose and fructose:
3) Glucose precursors:
Sodium propionate @ 80 gm PO for 3-6 days → slow response. Propylene glycol or glycerine @ 225 gm PO b.i.d. for 2 days followed by 110 g PO daily for 2 days.
4) Glucose orally:
Glucose 500 gm orally as drench following pre-medication with 30 gm sodium bicarbonate solution orally.
B) Hormonal Therapy:
1) Glucocorticoids:
Modern Treatment is dramatically successful. Dexamethasone @ 0.04 mg/kg I/V daily for 2-3 days. Steroids Decreased tissue uptake of glucose and promotes gluconeogenesis, reducing milk production for 3 days. Glucose + Corticosteroids Therapy is more effective than therapy with glucose or corticosteroids alone.
2) Insulin:
Glucose + Insulin (0.5 U/kg I/V or s/c) therapy is highly useful in cases of recurrent ketosis unresponsive to glucose or corticoid therapy. Insulin + Corticosteroid Therapy can also be used for the treatment of ketosis. Insulin **s**uppresses mobilization of fat and promotes glucose uptake by tissues, stimulating hepatic gluconeogenesis.
3) Anabolic Steroids: Durabolin / Trenbolone acetate 60-120 mg single dose. These steroids Stimulates appetite, decreases ketone body and FFA concentration and increases concentration of citrate in liver which helps in uptake of acetyl COA.
C) Miscellaneous Therapy:
1) Niacin @ 8 gm orally daily for 5-6 days Niacin is antilipolytic.
2) Cobalt sulphate @ 100 mg/day or vit. B_{12} 1-2 mg/kg i/m or i/v.
3) Vit. B_{12} converts propionate to glucose.
4) Chloral hydrate @ 30 g orally followed by 7gm daily for 3-5 days. It helps in the breakdown of starch in the rumen and stimulates the production of propionate and thereby increases the blood glucose level.

Supportive Treatment:

- ✧ Inj. liver extract with β-complex @ 5-10 ml I/m on alternate days.
- ✧ Provision of a mineral mixture comprising phosphorus and cobalt.

Differential Diagnosis

Wasting form of ketosis should be differentiated from diseases characterized by wasting / emaciation
1) Traumatic Reticulitis: Fever, recurrent tympany and evidence of pain. X-ray examination reveals a foreign body. No or transient response to treatment.
2) Traumatic Pericarditis: Fever, chest pain, brisket oedema. Muffled/splashing heart sounds. X-ray exam reveals a foreign body.
3) Vagal Indigestion /DH: Moderate frothy bloat not responding to treatment. Papple shaped abdominal distension.
4) Pneumonia / Pleurisy: Fever, chest pain, coughing, nasal discharge. Abnormal lung sounds.
5) Metritis: History of retention of placenta, dystocia, prolapse. Purulent vaginal discharge. P/R exam reveals swollen uterus.
6) Pyelonephritis: History of metritis. Fever, arching of the back and turbid urine. P/R reveals enlargement of the kidney.
7) Surra: Buffaloes are usually affected. Blood smear +ve for trypanosomes. Good response to Diminazene.
8) Theileriosis: Evidence of tick infestation. Persistent fever, enlargement of lymph nodes, anemia and Jaundice. Blood lymph smear positive for thieleria. Response to buparvaquone.
9) Diabetes mellitus: Hyperglycemia and ketonemia. Reduced glucose tolerance Good response to insulin therapy.
10) Abomasal displacement: Common in high producing recently calved dairy cows. Sudden anorexia, the building of abomasum, feces pasty and scantly, intermittent colic. Temporary response to glucose therapy.
The nervous form of ketosis should be differentiated from
1) Tetanus: Females and newborns are susceptible. Evidence of metritis or umbilical infections. Signs of tetany are more marked. No response to glucose therapy.
2) Rabies: History of dog bites. Profuse salivation, ascending paralysis. bellowing and change of voice followed by voiceless bellowing. No response to glucose therapy.
3) Encephalitis / Meningitis: Fever and rigidity of the neck. No response to glucose therapy
4) Lead poisoning: History of access to poison, Blindness and No response to glucose therapy

5) Pesticide poisoning: History access to poisoning. Slow response to intensive glucose therapy
6) Lactation tetany: History of grazing on green lush, pasture. Sudden onset, hyperaesthesia, preaching of ears, retraction of eyelids, retraction of eyelids.

Control:

Avoid either starvation or overfeeding at calving. So, animal should be neither thin nor over fat. Provide balanced ration to animals as per feeding standards. Give extra allowance of concentrate ration (protein 16%) during advance pregnancy (1.5 kg/day). After calving give the concentrate ration (protein 16%) depending upon the level of milk production i.e. 1 kg concentrate for every 2.5 – 3 kg of milk produced. Provide ground maize as it contains α-polymerized glucose which is not fermented in the rumen and is passed as such to the intestine and absorbed from there. Provide a ratio that increases propionate production and decreases acetate production. e.g. Finely ground roughage, cooked grains. Highly fermentable feeds such as molasses help to check ketosis. Provide whole cottonseed or soybean as a concentrated source of energy and glucogenic material. Provide a ration containing an adequate amount of phosphorus, cobalt and iodine. Avoid abrupt changes in the type of feed. Encourage maximum feed intake by providing palatable feed at frequent intervals. Give adequate exercise to lactating animals. Protect lactating animals from inclement weather viz. cold stress. Select cows/buffaloes having good feed capacity and appetite. Give the following glucose precursors in problem herds. Sodium propionate @ 110 g daily orally for 6 wks. Commencing at calving or Propylene glycol 200-400 ml daily from 5 days before to 10 days after calving. Carry out blood glucose estimations twice during the 2^{nd} – 6^{th} week of lactation to know the subclinical form of the disease. Perform Rothera's test on urine/milk samples at weekly intervals till 6-8 weeks after calving.